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added. The claims as amended are believed to avoid the rejections applied in the Final Office Action for reasons set forth more fully below.

The Office Action of April 10, 2001 has been received and carefully reviewed. It is submitted that, by this Amendment, all bases of rejection and objection are traversed and overcome. Upon entry of this Amendment, Claims 1-20, 22-38 and 40-44 remain in the application. New claims 45-47 have been added in order to set forth additional specific embodiments of Applicant's invention. Reconsideration of the claims as amended is requested.

At the outset, Applicant's Attorney sincerely thanks Examiner Sumesh Kaushal and SPE Deborah Clark for all the time and courtesies extended during the telephonic interview of June 5, 2001.

During the interview, the independent claims were discussed, more specifically claims 1 and 34. Further, the Draget, Cao and Hauselmann references were discussed at length. Examiner Clark suggested that the inclusion of language selectively controlling "shrinking, swelling or maintaining of the crosslinked hydrogel" (to replace controlling the hydrogel system to a "predetermined size") by varying a calcium ion concentration of [the] medium" would obviate the § 112, second paragraph rejections as long as such language was supported by the specification as filed (Applicant submits that such support may be found at page 16, lines 1-9).

During the interview, the Examiners acquiesced to the fact that none of Draget, Cao or Hauselmann taught or suggested control of swelling, shrinking or maintaining of a hydrogel by varying a cation concentration of a medium into which the hydrogel is introduced. As such, at the conclusion of the interview, Examiner Clark stated that if Applicant filed an amendment to overcome the § 112, second paragraph rejections by inclusion of language similar to that stated above, Examiner Kaushal would perform a further search and either allow the subject application or re-open prosecution.

Claims 1-10 and 23-33 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

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Applicant has included language similar to that suggested by the Examiner in each of the independent claims. As such, it is submitted that this rejection has been traversed and overcome.

Claims 1, 3-7, 9 and 23-28 stand rejected under 35 U.S.C. 102(a) as being anticipated by Draget et al (1991). Claims 2, 8, 10-20, 22 and 29-44 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Draget et al (1991) as applied to claims 1, 3-7, 9 and 23-28 above, and further in view of Hauselmann et al (US Patent 5,658,343) and Cao et al (1996).

Applicant affirms his arguments set forth in the previous amendment.

Independent claims 1, 11 and 23 had included a recitation that the size of the hydrogel was controlled by the calcium ion concentration of a medium into which the hydrogel was introduced. The subject matter of this recitation has also been introduced into independent claim 34. In order to obviate a § 112, second paragraph rejection, the "size" language was replaced by "shrinking, swelling or maintaining" per Examiner Clark's suggestion (as discussed above).

None of the cited references teach or suggest selective shrinking, swelling or maintaining of a hydrogel by varying cation concentration of a medium into the hydrogel is introduced. As such, it is submitted that Applicant's invention as defined in independent claims 1, 11, 23 and 34, as well as all claims dependent therefrom, is not anticipated, taught or rendered obvious by Draget, Cao or '343, either alone or in combination, and patentably defines over the art of record.

In summary, Claims 1-20, 22-38 and 40-44 remain in the application. Claims 1, 11, 23, 34, 40 and 41 have been amended. Claim 39 has been canceled. New claims 45-47 have been added in order to set forth additional specific embodiments of Applicant's invention. It is submitted that, through this amendment, Applicant's invention as set forth in these claims is now in a condition suitable for allowance.

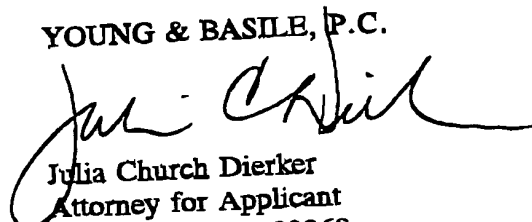
Further and favorable consideration is requested. If the Examiner believes it would expedite prosecution of the above-identified application, he is

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cordially invited to contact Applicant's Attorney at the below-listed telephone number.

Respectfully submitted,

YOUNG & BASILE, P.C.



Julia Church Dierker
Attorney for Applicant
Registration No. 33368
(248) 649-3333

3001 West Big Beaver Rd.
Suite 624
Troy, Michigan 48084
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VERSION OF CLAIM AMENDMENTS WITH MARKINGS
TO SHOW CHANGES MADE

- 1 1. (Three Times Amended) A method comprising the steps of:
2 mixing an alginate salt and a source of calcium ions to provide a
3 mixture;
4 adding a calcium releasing compound to the mixture to provide a
5 three-dimensional crosslinked hydrogel system; and
6 selectively controlling shrinking, swelling or maintaining of the
7 hydrogel system [to a predetermined size] by varying a calcium ion concentration
8 of a medium into which the hydrogel system is introduced.
- 1 11. (Three Times Amended) A method for tissue engineering *in*
2 *vitro*, the method comprising the steps of:
3 mixing cells, an alginate salt and a source of calcium ions to
4 provide a mixture;
5 adding a calcium releasing compound to the mixture to provide a
6 crosslinked hydrogel;
7 selectively controlling shrinking, swelling or maintaining of the
8 crosslinked hydrogel [system to a predetermined size] by varying a calcium ion
9 concentration of a medium into which the crosslinked hydrogel [system] is
10 introduced; and
11 culturing the crosslinked hydrogel in the medium to provide a
12 three-dimensional crosslinked hydrogel/cell system for growing the cells *in vitro*.
- 1 23. (Twice Amended) A method for preparing a three-dimensional
2 hydrogel system, the method comprising the steps of:
3 adding a cation-releasing compound to a mixture of at least one
4 hydrophilic polymer and a source of cations to provide a three-dimensional
5 crosslinked hydrogel system; and
6 selectively controlling shrinking, swelling or maintaining of the
7 hydrogel system [to a predetermined size] by varying a cation concentration of a

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8 medium into which the hydrogel system is introduced, wherein the cation in the
9 medium is selected to be the same cation as the cation in the hydrogel system.

1 34. (Twice Amended) A three-dimensional crosslinked hydrogel
2 composition, consisting essentially of:
3 at least one hydrophilic polymer;
4 a source of cations;
5 a cation-releasing compound, whereby a mixture of the at least one
6 hydrophilic polymer, the source of cations and the cation-releasing compound
7 forms the crosslinked hydrogel composition; and
8 [cells incorporated into the hydrogel composition, thereby forming a
9 hydrogel/cell system;]
10 a culture medium into which the hydrogel composition is
11 introduced, the culture medium having a predetermined cation concentration,
12 wherein the predetermined cation concentration determines the shrinking, swelling
13 or maintaining of the crosslinked hydrogel composition.

Please cancel claim 39 without prejudice.

1 40. (Amended) The composition as defined in claim [39] 34
2 wherein the cation in the medium is calcium, and wherein when the predetermined
3 cation concentration is a calcium ion concentration between about 0.0020 M and
4 about 0.0030 M, the hydrogel composition remains substantially the same size.

1 41. (Amended) The composition as defined in claim [34] 45
2 wherein the cells are at least one of osteoblasts and cells which secrete a medically
3 useful compound.

1 45. (New) The three-dimensional crosslinked hydrogel composition
2 as defined in claim 34, further comprising cells incorporated into the hydrogel
3 composition, thereby forming a hydrogel/cell system.

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1 46. (New) The three-dimensional crosslinked hydrogel composition
2 as defined in claim 34 wherein the cation in the medium is calcium, and wherein
3 when the predetermined cation concentration is a calcium ion concentration
4 between about 0.0005 M and about 0.0010 M, the hydrogel composition swelled.

1 47. (New) The three-dimensional crosslinked hydrogel composition
2 as defined in claim 34 wherein the cation in the medium is calcium, and wherein
3 when the predetermined cation concentration is a calcium ion concentration of
4 about 0.0040 M, the hydrogel composition shrank.